

Appl. No. 10/005,685
Amend. dated February 2, 2004
Reply to Office Action of August 1, 2003

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Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1-53. (canceled)

54. (currently amended) A method for extracting an analyte from a fluid sample, the method comprising the steps of:

- a) introducing the sample into a cartridge having:
 - i) a lysing chamber for lysing sample components to release the analyte therefrom, wherein the lysing chamber contains at least one filter for capturing the sample components by size exclusion as the sample flows through the lysing chamber; and
 - ii) an analyte capture region containing capture material for capturing the analyte;
- b) forcing the sample to flow through the lysing chamber to capture the sample components with the filter, wherein the volume of sample forced to flow through the lysing chamber is greater than the volume capacity of the lysing chamber;
- c) lysing the sample components in the lysing chamber to produce a lysate containing the analyte;
- d) forcing the lysate to flow through the capture region, thereby capturing the analyte with the capture material; and
- e) eluting the analyte from the capture region.

55. (previously presented) The method of claim 54, wherein the cartridge further includes a reaction chamber, and the method further comprises the steps of:

- i) forcing the eluted analyte to flow into the reaction chamber;
- ii) reacting the analyte in the reaction chamber; and

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- iii) detecting a reaction product.
56. (previously presented) The method of claim 55, wherein the analyte comprises nucleic acid, and wherein the steps of reacting the analyte and detecting the reaction product comprise amplifying the nucleic acid and detecting the amplified nucleic acid.
57. (currently amended) The method of claim 55, wherein the [[chemical]] reaction requires temperature control of the reaction chamber, the portion of the cartridge defining the reaction chamber protrudes from the rest of the cartridge body, and the method further comprises the steps of inserting the reaction chamber into a thermal sleeve and heating or cooling the reaction chamber according to a time/temperature profile.
58. (previously presented) The method of claim 55, wherein the cartridge further includes a reagent chamber containing dried or lyophilized reagents, and the method further comprises the step of mixing the eluted analyte with the reagents in the reagent chamber prior to forcing the analyte to flow into the reaction chamber.
59. (previously presented) The method of claim 54, further comprising the steps of:
- i) forcing the eluted analyte to flow into a reaction vessel coupled to the cartridge;
 - ii) reacting the analyte in the reaction vessel; and
 - iii) detecting a reaction product.
60. (previously presented) The method of claim 59, wherein the analyte comprises nucleic acid, and wherein the steps of reacting the analyte and detecting the reaction product comprise amplifying the nucleic acid and detecting the amplified nucleic acid.
61. (previously presented) The method of claim 59, wherein the reaction requires temperature control of the reaction vessel, and the method further comprises the steps of inserting the

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vessel into a thermal sleeve and heating or cooling the vessel according to a time/temperature profile.

62. (previously presented) The method of claim 59, wherein the cartridge further includes a reagent chamber containing dried or lyophilized reagents, and the method further comprises the step of mixing the eluted analyte with the reagents in the reagent chamber prior to forcing the analyte to flow into the reaction vessel.
63. (previously presented) The method of claim 54, wherein the step of lysing the sample components comprises transferring ultrasonic energy to the lysing chamber using an ultrasonic transducer coupled to a wall of the lysing chamber.
64. (canceled).
65. (previously presented) The method of claim 63, wherein the step of lysing the sample components further comprises agitating particles or beads in the lysing chamber to rupture the sample components.
66. (previously presented) The method of claim 63, further comprising the step of placing a lysis buffer in the lysing chamber, the lysis buffer containing a lysing reagent.
67. (previously presented) The method of claim 63, wherein the transducer comprises an ultrasonic horn for contacting the wall.
68. (previously presented) The method of claim 54, wherein the capture region comprises a channel or chamber containing the capture material, and the method further comprises the step of forcing a wash solution to flow through the capture region after the step of forcing

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the lysate to flow through the capture region and prior to eluting the analyte from the capture region.

69. (canceled).
70. (previously presented) The method of claim 54, wherein the capture region comprises a channel or chamber containing the capture material, and wherein the capture material comprises at least one solid support selected from the group consisting of filters, membranes, beads, fiber, glass wool, filter paper, polymers, and gel.
71. (previously presented) The method of claim 54, wherein the capture region comprises an extraction chamber formed in a microfluidic chip, and wherein the capture material comprises an array of microstructures extending into the extraction chamber, each of the microstructures having an aspect ratio (height to width) of at least 2:1.
72. (previously presented) The method of claim 54, wherein the capture region comprises a channel or chamber containing the capture material, and wherein the analyte is eluted from the capture region by heating the channel or chamber containing the capture material while forcing elution fluid to flow through the channel or chamber.
73. (previously presented) The method of claim 54, wherein the lysate is forced to recirculate through the capture region.
74. (previously presented) The method of claim 54, wherein the cartridge has a first flow path that includes the lysing and capture regions, the first flow path leading to a waste

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chamber, the cartridge has an elution flow path passing through the capture region and diverging from the first flow path, the lysate is forced to flow through the capture region and into the waste chamber via the first flow path, and the elution fluid is forced to flow through the capture region and along the diverging elution flow path.

75. (previously presented) The method of claim 54, wherein the analyte is eluted from the capture region by forcing elution fluid to flow through the capture region, and wherein the volume of sample forced to flow through the lysing chamber is greater than the volume of elution fluid forced to flow through the capture region, whereby the analyte extracted from the sample is concentrated in the smaller volume of elution fluid.
76. (canceled).
77. (previously presented) The method of claim 54, wherein the ratio of the volume of sample forced to flow through the lysing chamber to the volume capacity of the lysing chamber is at least 2:1.
78. (previously presented) The method of claim 54, wherein the volume of sample forced to flow through the lysing chamber is at least 1 ml.
79. (previously presented) The method of claim 54, wherein the capture region comprises an extraction chamber containing the capture material, and wherein the volume of lysate forced to flow through the extraction chamber is greater than the volume capacity of the extraction chamber.
80. (previously presented) The method of claim 79, wherein the ratio of the volume of lysate forced to flow through the extraction chamber to the volume capacity of the extraction

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chamber is at least 2:1.

81. (currently amended) A method for extracting nucleic acid from a fluid sample and for amplifying the nucleic acid, the method comprising the steps of:
- a) introducing the sample into a cartridge having:
 - i) a lysing chamber for lysing sample components to release the nucleic acid therefrom, wherein the lysing chamber contains solid phase material for capturing the sample components as the sample flows through the lysing chamber;
 - ii) a capture region [[, the capture region]] comprising a channel or chamber containing capture material for capturing the nucleic acid;
 - iii) at least one waste chamber; and
 - iv) a reaction chamber for amplifying the nucleic acid;
 - b) forcing the sample to flow through the lysing chamber and into the at least one waste chamber to capture the sample components with the solid phase material, wherein the volume of sample forced to flow through the lysing chamber is greater than the volume capacity of the lysing chamber;
 - c) lysing the sample components in the lysing chamber to produce a lysate containing the nucleic acid;
 - d) forcing the lysate to flow through the capture region, thereby capturing the nucleic acid with the capture material;
 - e) forcing the lysate that has flowed through the capture region to flow into the waste chamber;
 - f) forcing an elution fluid to flow through the capture region to elute the captured nucleic acid from the capture region;
 - g) forcing the eluted nucleic acid to flow into the reaction chamber; and

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- h) amplifying the nucleic acid in the reaction chamber, wherein the temperature of the reaction chamber is controlled by inserting the reaction chamber into a thermal sleeve and heating or cooling the reaction chamber according to a time/temperature profile.
82. (previously presented) The method of claim 81, further comprising the step of detecting the amplified nucleic acid in the reaction chamber.
83. (canceled)
84. (previously presented) The method of claim 81, wherein the cartridge further includes a reagent chamber containing dried or lyophilized reagents, and the method further comprises the step of mixing the eluted nucleic acid with the reagents in the reagent chamber prior to forcing the nucleic acid to flow into the reaction chamber.
85. (previously presented) The method of claim 81, wherein the lysate is forced to recirculate through the capture region prior to being forced to flow into the waste chamber.
86. (previously presented) The method of claim 81, wherein the step of lysing the sample components comprises transferring ultrasonic energy to the lysing chamber using an ultrasonic transducer coupled to a wall of the lysing chamber.
87. (previously presented) The method of claim 86, wherein the solid phase material comprises at least one membrane or filter for capturing the sample components, and wherein the step of lysing the sample components further comprises agitating particles or beads in the lysing chamber to rupture the sample components.

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88. (previously presented) The method of claim 86, wherein the step of lysing the sample components further comprises placing a lysis buffer in the lysing chamber, the lysis buffer containing a lysing reagent.
89. (previously presented) The method of claim 86, wherein the transducer comprises an ultrasonic horn for contacting the wall of the lysing chamber.
90. (previously presented) The method of claim 81, wherein the volume of sample forced to flow through the lysing chamber is greater than the volume of elution fluid forced to flow through the capture region, whereby the nucleic acid extracted from the sample is concentrated in the smaller volume of elution fluid.
91. (canceled).
92. (previously presented) The method of claim 81, wherein the ratio of the volume of sample forced to flow through the lysing chamber to the volume capacity of the lysing chamber is at least 2:1.
93. (previously presented) The method of claim 81, wherein the volume of sample forced to flow through the lysing chamber is at least 1 ml.
94. (previously presented) The method of claim 81, wherein the volume of lysate forced to flow through the capture region is greater than the volume capacity of the capture region.
95. (previously presented) The method of claim 81, wherein the ratio of the volume of lysate forced to flow through the capture region to the volume capacity of the capture region is at least 2:1.

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96. (previously presented) The method of claim 81, wherein the capture material comprises at least one solid support selected from the group consisting of filters, membranes, beads, fiber, glass wool, filter paper, polymers, and gel.
97. (previously presented) The method of claim 81, wherein the capture region comprises an extraction chamber formed in a microfluidic chip, and wherein the capture material comprises an array of microstructures extending into the extraction chamber, each of the microstructures having an aspect ratio (height to width) of at least 2:1.
98. (previously presented) The method of claim 81, further comprising the step of heating the capture region while forcing the elution fluid to flow through the capture region.
99. (currently amended) A method for separating nucleic acid from a fluid sample and for amplifying the nucleic acid, the method comprising the steps of:
- a) introducing the sample into a cartridge having:
 - i) a lysing chamber for lysing sample components to release the nucleic acid therefrom, wherein the lysing chamber contains solid phase material for capturing the sample components as the sample flows through the lysing chamber;
 - ii) a capture region comprising a channel or chamber containing capture material for capturing the nucleic acid; and
 - iii) at least one waste chamber;
 - b) forcing the sample to flow through the lysing chamber and into the at least one waste chamber to capture the sample components with the solid phase material, wherein the volume of sample forced to flow through the lysing chamber is greater than the volume capacity of the lysing chamber;

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- c) lysing the sample components in the lysing chamber to produce a lysate containing the nucleic acid;
 - d) forcing the lysate to flow through the capture region, thereby capturing the nucleic acid with the capture material in the capture region;
 - e) forcing the lysate that has flowed through the capture region to flow into the waste chamber;
 - f) forcing an elution fluid to flow through the capture region to elute the captured nucleic acid from the capture region;
 - g) forcing the eluted nucleic acid to flow into a reaction vessel coupled to the cartridge; and
 - h) amplifying the nucleic acid in the reaction vessel, wherein the temperature of the reaction vessel is controlled by inserting the vessel into a thermal sleeve and heating or cooling the vessel according to a time/temperature profile.
100. (previously presented) The method of claim 99, further comprising the step of detecting the amplified nucleic acid in the reaction vessel.
101. (canceled)
102. (previously presented) The method of claim 99, wherein the cartridge further includes a reagent chamber containing dried or lyophilized reagents, and the method further comprises the step of mixing the eluted nucleic acid with the reagents in the reagent chamber prior to forcing the nucleic acid to flow into the reaction vessel.
103. (previously presented) The method of claim 99, wherein the lysate is forced to recirculate through the capture region prior to being forced to flow into the waste chamber.

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104. (previously presented) The method of claim 99, wherein the step of lysing the sample components comprises transferring ultrasonic energy to the lysing chamber using an ultrasonic transducer coupled to a wall of the lysing chamber.
105. (previously presented) The method of claim 104, wherein the solid phase material comprises at least one membrane or filter for capturing the sample components, and wherein the step of lysing the sample components further comprises agitating particles or beads in the lysing chamber to rupture the sample components.
106. (previously presented) The method of claim 104, wherein the step of lysing the sample components further comprises placing a lysis buffer in the lysing chamber, the lysis buffer containing a lysing reagent.
107. (previously presented) The method of claim 104, wherein the transducer comprises an ultrasonic horn for contacting the wall of the lysing chamber.
108. (previously presented) The method of claim 99, wherein the volume of sample forced to flow through the lysing chamber is greater than the volume of elution fluid forced to flow through the capture region, whereby the nucleic acid extracted from the sample is concentrated in the smaller volume of elution fluid.
109. (canceled).
110. (previously presented) The method of claim 99, wherein the ratio of the volume of sample forced to flow through the lysing chamber to the volume capacity of the lysing chamber is at least 2:1.

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111. (previously presented) The method of claim 99, wherein the volume of sample forced to flow through the lysing chamber is at least 1 ml.
112. (previously presented) The method of claim 99, wherein the volume of lysate forced to flow through the capture region is greater than the volume capacity of the capture region.
113. (previously presented) The method of claim 99, wherein the ratio of the volume of lysate forced to flow through the capture region to the volume capacity of the capture region is at least 2:1.
114. (previously presented) The method of claim 99, wherein the capture material comprises at least one solid support selected from the group consisting of filters, membranes, beads, fiber, glass wool, filter paper, polymers, and gel.
115. (previously presented) The method of claim 99, wherein the capture region comprises an extraction chamber formed in a microfluidic chip, and wherein the capture material comprises an array of microstructures extending into the extraction chamber, each of the microstructures having an aspect ratio (height to width) of at least 2:1.
116. (previously presented) The method of claim 99, further comprising the step of heating the capture region while forcing the elution fluid to flow through the capture region.
117. (previously presented) A method for extracting nucleic acid from a fluid sample and for amplifying the nucleic acid, the method comprising the steps of:
 - a) introducing the sample into a cartridge having:
 - i) a capture region, the capture region comprising a channel or chamber

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- containing capture material for capturing the nucleic acid; and
- ii) a waste chamber for receiving waste fluid from the capture region;
- b) forcing the sample to flow through the capture region, thereby extracting the nucleic acid from the sample with the capture material in the capture region;
 - c) forcing the remaining sample fluid that has flowed through the capture region to flow into the waste chamber;
 - d) forcing an elution fluid to flow through the capture region to elute the captured nucleic acid from the capture region;
 - e) forcing the eluted nucleic acid to flow into a reaction vessel coupled to the cartridge; and
 - f) amplifying the nucleic acid in the reaction vessel, wherein the temperature of the reaction vessel is controlled by inserting the vessel into a thermal sleeve and heating or cooling the vessel according to a time/temperature profile.
118. (previously presented) The method of claim 117, further comprising the step of detecting the amplified nucleic acid in the reaction vessel.
119. (previously presented) The method of claim 117, wherein the sample is forced to recirculate through the capture region prior to being forced to flow into the waste chamber.
120. (previously presented) The method of claim 117, wherein the cartridge further includes a reagent chamber containing dried or lyophilized reagents, and the method further comprises the step of mixing the eluted nucleic acid with the reagents in the reagent chamber prior to forcing the nucleic acid to flow into the reaction vessel.

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121. (previously presented) The method of claim 117, wherein the volume of sample forced to flow through the capture region is greater than the volume of elution fluid forced to flow through the capture region, whereby the nucleic acid extracted from the sample is concentrated in the smaller volume of elution fluid.
122. (previously presented) The method of claim 117, wherein the ratio of the volume of sample forced to flow through the capture region to the volume capacity of the capture region is at least 2:1.
123. (previously presented) The method of claim 117, wherein the volume of sample forced to flow through the capture region is at least 1 ml.
124. (previously presented) The method of claim 117, wherein the capture material comprises at least one solid support selected from the group consisting of filters, membranes, beads, fiber, glass wool, filter paper, polymers, and gel.
125. (previously presented) The method of claim 117, wherein the capture region comprises an extraction chamber formed in a microfluidic chip, and wherein the capture material comprises an array of microstructures extending into the extraction chamber, each of the microstructures having an aspect ratio (height to width) of at least 2:1.
126. (previously presented) A method for extracting nucleic acid from a fluid sample and for amplifying the nucleic acid, the method comprising the steps of:
- a) introducing the sample into a cartridge having:
 - i) a flow path through a capture region, the capture region comprising a channel or chamber containing capture material for capturing the nucleic acid;

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- ii) a waste chamber for receiving waste fluid from the capture region; and
 - iii) a reaction chamber for amplifying the nucleic acid;
 - b) forcing the sample to flow through the capture region, thereby capturing the nucleic acid with the capture material;
 - c) forcing the remaining sample fluid that has flowed through the capture region to flow into the waste chamber;
 - d) forcing an elution fluid to flow through the capture region to elute the captured nucleic acid from the capture region;
 - e) forcing the eluted nucleic acid to flow into the reaction chamber; and
 - f) amplifying the nucleic acid in the reaction chamber, wherein the temperature of the reaction chamber is controlled by inserting the reaction chamber into a thermal sleeve and heating or cooling the reaction chamber according to a time/temperature profile.
127. (previously presented) The method of claim 126, further comprising the step of detecting the amplified nucleic acid in the reaction chamber.
128. (previously presented) The method of claim 126, wherein the sample is forced to recirculate through the capture region prior to being forced to flow into the waste chamber.
129. (previously presented) The method of claim 126, wherein the cartridge further includes a reagent chamber containing dried or lyophilized reagents, and the method further comprises the step of mixing the eluted nucleic acid with the reagents in the reagent chamber prior to forcing the nucleic acid to flow into the reaction chamber.

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130. (previously presented) The method of claim 126, wherein the volume of sample forced to flow through the capture region is greater than the volume of elution fluid forced to flow through the capture region, whereby the nucleic acid extracted from the sample is concentrated in the smaller volume of elution fluid.
131. (previously presented) The method of claim 126, wherein the volume of sample forced to flow through the capture region is greater than the volume capacity of the capture region.
132. (previously presented) The method of claim 126, wherein the ratio of the volume of sample forced to flow through the capture region to the volume capacity of the capture region is at least 2:1.
133. (previously presented) The method of claim 126, wherein the volume of sample forced to flow through the capture region is at least 1 ml.
134. (previously presented) The method of claim 126, wherein the capture material comprises at least one solid support selected from the group consisting of filters, membranes, beads, fiber, glass wool, filter paper, polymers, and gel.
135. (previously presented) The method of claim 126, wherein the capture region comprises an extraction chamber formed in a microfluidic chip, and wherein the capture material comprises an array of microstructures extending into the extraction chamber, each of the microstructures having an aspect ratio (height to width) of at least 2:1.
136. (previously presented) The method of claim 126, further comprising the step of heating the capture region while forcing the elution fluid to flow through the capture region.

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137-214. (canceled)

215. (previously presented) A method for separating an analyte from a fluid sample, the method comprising the steps of:
- a) introducing the sample into a cartridge having:
 - i) a lysing region for lysing sample components to release the analyte therefrom; and
 - ii) a flow-through chip for capturing the analyte, the chip comprising a body having an extraction chamber and an array of microstructures extending into the extraction chamber for capturing the analyte, wherein each of the microstructures has an aspect ratio (height to width) of at least 2:1;
 - b) lysing the sample components in the lysing region;
 - c) forcing the lysed sample to flow through the extraction chamber and out of the chip, thereby capturing the analyte with the microstructures in the extraction chamber;
 - d) eluting the captured analyte from the chip by forcing an elution fluid to flow through the extraction chamber and out of the chip.
216. (previously presented) The method of claim 215, wherein the cartridge further includes a reaction chamber, and the method further comprises the steps of:
- i) forcing the eluted analyte to flow into the reaction chamber;
 - ii) reacting the analyte in the reaction chamber; and
 - iii) detecting a reaction product.
217. (previously presented) The method of claim 216, wherein the analyte comprises nucleic acid, and wherein the steps of reacting the analyte and detecting the reaction product comprise amplifying the nucleic acid and detecting the amplified nucleic acid.

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218. (previously presented) The method of claim 216, wherein the cartridge further includes a reagent chamber containing dried or lyophilized reagents, and the method further comprises the step of mixing the nucleic acid with the reagents in the reagent chamber prior to forcing the nucleic acid to flow into the reaction chamber.
219. (previously presented) The method of claim 215, further comprising the steps of:
- i) forcing the eluted analyte to flow into a reaction vessel coupled to the cartridge;
 - ii) reacting the analyte in the reaction vessel; and
 - iii) detecting a reaction product.
220. (previously presented) The method of claim 219, wherein the analyte comprises nucleic acid, and wherein the steps of reacting the analyte and detecting the reaction product comprise amplifying the nucleic acid and detecting the amplified nucleic acid.
221. (previously presented) The method of claim 219, wherein the cartridge further includes a reagent chamber containing dried or lyophilized reagents, and the method further comprises the step of mixing the eluted nucleic acid with the reagents in the reagent chamber prior to forcing the nucleic acid to flow into the reaction vessel.
222. (previously presented) The method of claim 215, wherein the step of lysing the sample components comprises transferring ultrasonic energy to the lysing region using an ultrasonic transducer coupled to a wall of the lysing region.
223. (previously presented) The method of claim 215, wherein the volume of sample forced to flow through the extraction chamber is greater than the volume of elution fluid forced to flow through the extraction chamber, whereby the analyte extracted from the sample is concentrated in the smaller volume of elution fluid.

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224. (previously presented) The method of claim 215, wherein the volume of sample forced to flow through the extraction chamber is greater than the volume capacity of the extraction chamber.
225. (previously presented) The method of claim 215, wherein the ratio of the volume of sample forced to flow through the extraction chamber to the volume capacity of the extraction chamber is at least 2:1.
226. (previously presented) The method of claim 215, wherein the volume of sample forced to flow through the extraction chamber is at least 1 ml.
227. (previously presented) The method of claim 117, further comprising the step of lysing the sample prior to forcing the lysed sample to flow through the capture region.
228. (previously presented) The method of claim 126, further comprising the step of lysing the sample prior to forcing the lysed sample to flow through the capture region.
229. (previously presented) The method of claim 216, wherein the reaction requires temperature control of the reaction chamber, and the method further comprises the steps of inserting the reaction chamber into a thermal sleeve and heating or cooling the reaction chamber according to a time/temperature profile.
230. (previously presented) The method of claim 219, wherein the reaction requires temperature control of the reaction vessel, and the method further comprises the steps of inserting the vessel into a thermal sleeve and heating or cooling the vessel according to a time/temperature profile.